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| 10/099,818      | 03/14/2002  | Iqbal Grewal         | P1824R1             | 2744             |

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| EXAMINER |
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GAMBEL, PHILLIP

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| ART UNIT | PAPER NUMBER |
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1644

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE  | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS                               | 03/12/2007 | PAPER         |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

|                              |                               |                               |  |
|------------------------------|-------------------------------|-------------------------------|--|
| <b>Office Action Summary</b> | Application No.<br>10/099,818 | Applicant(s)<br>GREWAL, IQBAL |  |
|                              | Examiner<br>Phillip Gambel    | Art Unit<br>1644              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10/5/06; 12/14/06.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13-30, 32 and 33 is/are pending in the application.
- 4a) Of the above claim(s) 19-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13-18, 32-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 12/14/06, has been entered.

Applicant's amendment, filed 10/5/06, has been entered.

Claims 1, 9, 11, 15 and 18 have been amended.

Claims 32-33 have been added.

Claims 12 and 31 have been canceled.

Claims 1-11, 13-30 and 32-33 are pending.

As pointed out previously, applicant's election of Group I and the species of a CD40-specific antibody and a CD20-specific antibody as well as multiple myeloma in the reply filed on 11/14/05 has been acknowledged.

Also, as pointed out previously, claims 1-11, 13-18 and 32-33 are under consideration in this application as they read on CD40-specific antibodies and CD20-specific antibodies as the specific agents as well as the various neoplastic diseases claimed in the interest of compact prosecution.

Claims 19-30 have been withdrawn from consideration as being drawn to the non-elected species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Action will be in response to applicant's amendment, filed 10/5/06.

In addition, given the entry of applicant's amendment / arguments, filed 10/5/06, New Grounds of Rejection have been set forth herein with respect to the recitation of:

"an effective amount of a combination of a CD40 specific binding agent and a CD20 specific binding agent, wherein said combination is sufficient for therapeutically effective treatment of said neoplastic disease or disorder in said mammal".

Art Unit: 1644

3. Given applicant's newly amended claims which now recite:

"an effective amount of a combination of a CD40 specific binding agent and a CD20 specific binding agent, wherein said combination is sufficient for therapeutically effective treatment of said neoplastic disease or disorder in said mammal"

and the new matter issues under 35 USC 112, first paragraph, presented herein, the priority of the instant claims is not deemed to be the filing date of the priority application USSN 60/280,805, filed 4/2/01.

4. The previous rejections under 35 U.S.C. § 112, first and second paragraphs, with respect to the recitation of "a CD40 agonist" have been withdrawn in view of applicant's amendment / amended claims, filed 10/5/06.

5. The previous rejections under 35 U.S.C. § 112, first and second paragraphs, with respect to the recitation of "S2C6", "C2B8" and "rituximab have been withdrawn in view of applicant's amendment / amended claims, filed 10/5/06.

Also, see U.S. Patent No. 5,736,137 (Anderson et al., anti-CD20 antibody) and U.S. Patent No. 6,843,989 (Siegall et al., anti-CD40 antibody) for satisfying the requirements for the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

It is noted that applicant has not provided objective evidence of the commercial availability of the claimed antibodies.

6. Given applicant's amendment to the instant disclosure deleting the description of "S2C6 comprises VL amino acid sequences of SEQ ID NO: 1 and SEQ ID NO: 2 and the VH amino acid sequences of SEQ ID NO. 6 and SEQ IDNO: 7 of WO 00/75348" on page 20 of the instant specification,

the previous objection to the amendment filed 2/28/06 under 35 U.S.C. 132 and the previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter have been withdrawn

7. Claims 1-11, 13-18 and 32-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11, 13-18 and 32-33 are indefinite in the recitation of "an effective amount of a combination of a CD40 specific binding agent and a CD20 specific binding agent, wherein said combination is sufficient for therapeutically effective treatment of said neoplastic disease or disorder in said mammal" because this "limitation" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Art Unit: 1644

It is further noted that applicant's arguments to distinguish the instant methods from the prior art relies primarily on this claim limitation, even though the specification as-filed failing to particularly point out and distinctly claim or set forth the metes and bounds of this "effective amount of a combination ...", which applicant regards as the invention.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

8. This is a written description / new matter rejection under 35 U.S.C. § 112, first paragraph.

Claims 1-11, 13-18 and 32-33 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:

"an effective amount of a combination of a CD40 specific binding agent and a CD20 specific binding agent, wherein said combination is sufficient for therapeutically effective treatment of said neoplastic disease or disorder in said mammal".

Applicant's amendment, filed 10/5/06, directs supports for "effective amount of a combination" mostly to Figures 4 and 5 (as well as pages 5, 20 and 21 of the specification).

However, Figures 4 and 5 and the Examples (e.g., see pages 44-46 of the instant specification) are limited to the particular combination of anti-CD20 antibody (RITUXAN) and an anti-CD40 antibody (SGN-14) in a particular dosing regimen (100 µg per mouse three (3) times per week for three weeks in experimental SCID models and testing anti-tumor activity against experimental tumors (H.S. Sultan myeloma and Ramos lymphoma).

However, the specification does not provide a definition of the claimed "effective amount of a combination", nor provides a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds or scope of the claimed invention.

Further, it is noted that applicant's reliance on this claimed "effective amount of a combination" as a means to distinguish the instant claimed methods from the prior art appears inconsistent with the disclosure as filed, which discloses the following.

"The term "therapeutically effective amount" is used to refer to an amount of an active agent having a growth arrest effect or causes the deletion of the cell. ... "

See page 17, paragraph 4 of the instant specification.

Art Unit: 1644

"Depending on the type and severity of the disease, about 1 µg/kg to 15 mg/kg (e.g. 1-20 mg/kg) of antibody is an initial candidate dosage for administration to the patient ... and a typical daily dosage might range from about 1 µg/kg to 100 mg/kg or more depending on the factor mentioned above. ... the treatment is sustained until a desired suppression of the disease symptoms occurs ...".

See page 43, paragraph 4 of the instant specification.

Applicant's reliance on generic disclosure of "therapeutically effective amounts", broad dosage ranges depending on the severity of the disease and possibly a single or limited species of particular dosages in experimental SCID mice does not provide sufficient direction and guidance to the "features/limitations" currently claimed. It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

The newly added recitation of "an effective amount of a combination ..." is not supported by the specification as-filed.

Therefore, the specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide sufficient blaze marks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.

See MPEP 714.02 and 2163.06

For examination purposes, the claimed "effective amount of a combination ..." will be given its broadest reasonable interpretation, which is consistent with the instant disclosure as filed (e.g., see page 17, paragraph 4 and page 43, paragraph 4 of the instant specification addressed above).

Art Unit: 1644

9. Claims 1-11, 13-18 and 32-33 are rejected under 35 U.S.C. § 102(e) as anticipated by Hanna et al. (US 2001/0018041 A1) (see entire document) and in further evidence of Armitage et al. (U.S. Patent No. 5,674,492 cited in paragraphs [0013] and [0104] of Hanna et al.), wherein said teachings of agonistic anti-CD40 are acknowledged by page 2, paragraph 1 of the instant specification and paragraphs [0005] and [0036] of Fanslow et al., US 2005/0129689 A1) essentially for the reasons of record.

Applicant's arguments, filed 10/5/06, in conjunction with certain legal citations, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant argues that a reference must teach each and every element in the claim to anticipate and that the prior art fails to teach claimed therapeutic effective amounts of the combination of anti-CD40 and anti-CD20 antibodies.

In contrast to applicant's arguments and as pointed out above, the instant claims, including the effective amounts and the "effective amounts of the combination", are given their broadest reasonable interpretation as they broadly read on effective amounts of treating neoplastic diseases.

Also, as indicated above, given the failure to particularly point out and distinctly claim or set forth the metes and bounds of this "effective amount of a combination ...",

The claimed effective amounts are broad and read on therapeutic effects amounts of anti-CD40 antibodies and anti-CD20 antibodies and are not limited to any particular dosage per se, other than what appears to be effective amounts known, practiced and taught by the prior art in therapeutic regimens, including the treatment of the same or nearly the same neoplastic diseases or disorders encompassed by the instant claims.

Also, as note above, this broadest reasonable interpretation is consistent with the instant disclosure as filed.

For example, Hanna et al. teach effective amounts can be determined by standard techniques well known to those of ordinary skill in the art and factors influencing dosages as well as specific dosage ranges (e.g., see paragraphs [0071] – [0078] and [0107] ) consistent with the instant disclosure (e.g., see page 17, paragraph 4 and page 43, paragraph 4 of the instant specification).

Further, it is noted that the prior art is directed towards effective treatment of the same malignancies with the same anti-CD40 antibodies and anti-CD20 antibodies encompassed by the instant claims.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001

Art Unit: 1644

On this record, it is reasonable to conclude that the same patient in need is being administered the same neutralizing anti-CD40 antibodies and anti-CD20 antibodies to treat various neoplastic disorders and diseases by the same mode of administration in the same or nearly the same effective amounts in both the instant claims and the prior art reference.

While applicant submits that Hanna focuses on the use of anti-CD40L antibodies and antagonists, Hanna is not limited to this particular agent to treat malignancies.

Applicant is reminded that Hanna also contemplates the particular combination of anti-CD20 antibodies and anti-CD40 antibodies. See paragraph [0104] on page 10 of Hanna.

Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts.

See MPEP 2111.03.

Therefore, the instant claims are met by any prior teaching of combining anti-CD40L antibodies with anti-CD20 and anti-CD40 antibodies, as broadly encompassed by the claimed methods.

Applicant's arguments have not been found persuasive

The following of record is reiterated for applicant's convenience.

Hanna et al. teach methods of treating B cell lymphomas and leukemias, including non-Hodgkin's lymphoma (NHL) (e.g. see paragraphs [0090] – [0101]) with the combination of CD40-specific antibodies (e.g. see CD40L Antagonists in paragraphs [0036] – [0078], and CD20-specific antibodies, including the C2B8 antibody / Rituxan (e.g. see paragraph [0104]) (e.g. see paragraphs Summary of the Invention, including paragraph [0018]; Detailed Description of the invention, including paragraphs [0088], [0092], [0104] and [0113]; Claims). Although the prior art does not teach the CD40-specific S2C6 antibody per se, the inhibitory CD40-specific antibodies taught by the prior art would have the same CD40 binding characteristics under the broadest reasonable interpretation of CD40-binding antibodies in the absence of limitations to the contrary.

Paragraphs [0013] and [0104] of Hanna et al. contemplates the anti-CD40 antibodies taught by Armitage et al. (U.S. Patent No. 5,674,492).

Armitage et al. teach anti-CD40 antibodies, including the M2 and M3 antibodies (See entire document).



Art Unit: 1644

For example, page 2, paragraph 1 of the instant specification discloses that:  
"CD40 stimulation by mAb M2 and M3 inhibits growth of several B-cell lymphomas and induces regression of several B-cell lymphomas and induces regression of established tumors in vivo (Funakoshi et al., (1994) Blood 83: 2787-2794; Funakoshi et al. J. Immunol., (1996) 19: 93-101).

Fanslow et al. US 2005/0129689 A1) describes the antibodies referenced in U.S. Patent No. 5,674,492, namely the M2 and M3 antibodies as agonistic anti-CD40 antibodies as those antibodies that mimic the biological effects of CD40L are useful in the treatment of disease characterized by neoplastic cells that express CD40 such as B lymphomas, melanomas and carcinomas,

Again, certain anti-CD40 antibodies referenced by Hanna et al. are the same anti-CD40 antibodies taught by U.S. Patent No. 5,674,492, which is referenced in paragraphs [0013] and [0104] of Hanna et al.

Therefore, Hanna et al. does teach the use of anti-CD40 antibodies, including its combination with anti-CD20 antibodies, in the treatment of B cell lymphomas and leukemias.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001

On this record, it is reasonable to conclude that the same patient in need is being administered the same neutralizing anti-CD40 and anti-CD20 antibodies to treat various neoplastic disorders and diseases by the same mode of administration in the same or nearly the same effective amounts in both the instant claims and the prior art reference.

Again, applicant's arguments have not been found persuasive.

10. Claims 1-11, 13-18 and 32-33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hanna et al. (US 2001/0018041 A1) in view of Siegall et al. (U.S. Patent No. 6,843,989) and Grillo-Lopez (U.S. Patent No. 6,455,043) and in further view of Armitage et al. (U.S. Patent No. 5,674,492 cited in paragraphs [0013] and [0104] of Hanna et al.) and Benoit et al. (Immunopharmacology 35: 129-139, 1996) (1449; #59),

and in further evidence of the referenced teachings of agonistic anti-CD40 are acknowledged by page 2, paragraph 1 of the instant specification and paragraphs [0005] and [0036] of Fanslow et al., US 2005/0129689 A1) essentially for the reasons of record.

Art Unit: 1644

Applicant's arguments, filed 10/5/06, have been fully considered but are not found convincing essentially for the reasons of record and addressed above in the rejection under 35 USC 102.

In contrast to applicant's assertions concerning the lack of teaching the combination of anti-CD40 antibodies and anti-CD20 antibodies in the treatment of neoplastic diseases or disorders or "an effective amount of said combination ..."

and as pointed out above,

the instant claims, including the effective amounts and the "effective amounts of the combination", are given their broadest reasonable interpretation as they broadly read on effective amounts of treating neoplastic diseases.

Also, as indicated above, given the failure to particularly point out and distinctly claim or set forth the metes and bounds of this "effective amount of a combination ...",

The claimed effective amounts are broad and read on therapeutic effects amounts of anti-CD40 antibodies and anti-CD20 antibodies and are not limited to any particular dosage per se, other than what appears to be effective amounts known, practiced and taught by the prior art in therapeutic regimens, including the treatment of the same or nearly the same neoplastic diseases or disorders encompassed by the instant claims.

Also, as noted above, this broadest reasonable interpretation is consistent with the instant disclosure as filed.

For example, Hanna et al. teach effective amounts can be determined by standard techniques well known to those of ordinary skill in the art and factors influencing dosages as well as specific dosage ranges (e.g., see paragraphs [0071] – [0078] and [0107] ) consistent with the instant disclosure (e.g., see page 17, paragraph 4 and page 43, paragraph 4 of the instant specification).

While applicant submits that Hanna focuses on the use of anti-CD40L antibodies and antagonists, Hanna is not limited to this particular agent to treat malignancies.

Applicant is reminded that Hanna also contemplates the particular combination of anti-CD20 antibodies and anti-CD40 antibodies. See paragraph [0104] on page 10 of Hanna.

Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts.

See MPEP 2111.03.

Therefore, the instant claims are met by any prior teaching of combining anti-CD40L antibodies with anti-CD20 and anti-CD40 antibodies, as broadly encompassed by the claimed methods.

Applicant's arguments have not been found persuasive

Art Unit: 1644

Further, it is noted that the prior art is directed towards effective treatment of the same malignancies with the same anti-CD40 antibodies and anti-CD20 antibodies encompassed by the instant claims.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001

On this record, it is reasonable to conclude that the same patient in need is being administered the same neutralizing anti-CD40 and anti-CD20 antibodies to treat various neoplastic disorders and diseases by the same mode of administration in the same or nearly the same effective amounts in both the instant claims and the prior art reference.

The following of record is reiterated for applicant's convenience.

Siegall methods of treating cancer, including leukemias, lymphomas (e.g. non-Hodgins lymphoma), solid tumor and multiple myeloma (e.g. see Therapeutic Uses, including Table 1 on columns 22-23 and Claims) with CD40-specific antibodies, including the S2C6 CD40-specific antibody of the instant invention (see entire document, including Claims)

Grillo-Lopez also teach treating various tumors with CD20-specific antibodies (See entire document) and teachings the expression of CD20 on multiple myeloma (e.g. see columns 15-16, overlapping paragraph) in addition to leukemias and lymphomas (e.g. see Field of the Invention on column 1 and Detailed Description of the Invention and Claims).

Benoit et al. was provided to address applicant's arguments concerning motivation of combining anti-CD40 antibodies with anti-CD20 antibodies in the treatment of B cell lymphomas.

Benoit et al. teach the increased inhibition of proliferation of B cell lymphomas following ligation of CD40, and CD20, for example (see entire document, including Abstract and Discussion).

The anti-CD40 antibody was the known G28-5 anti-CD40 antibody (see Antibodies and reagents on page 130, column 2).

Art Unit: 1644

Given both the therapeutic use of CD40-specific antibodies and CD20-specific antibodies to treat various neoplastic diseases, including leukemias, lymphomas, myelomas and solid tumors, the ordinary artisan would have been motivated to combine the two antibody specificities as taught by Hanna et al. in combination therapies to target other neoplastic tissues in order to increase the efficacy of cancer treatment. As taught by all of the prior art references, combination therapies, including combination with antibodies or combination of antibodies with more traditional chemotherapy and radiotherapy were well known and practiced by the ordinary artisan at the time the invention was made to increase efficacy of treatment and to minimize toxic effects of such treatment in order to meet the needs of the patients (see Detailed Descriptions of Hanna et al., Siegall and Grillo-Lopez). From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as pointed out previously in response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case the teachings of the prior art do provide for the use of anti-CD40 antibodies in the treatment of certain neoplastic disorders and diseases and do indicate success in treating neoplastic disorders and diseases with anti-CD40 antibodies in combination with anti-CD20 antibodies that would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

Again, applicant's arguments have not been found persuasive as being inconsistent with the clear teachings of the prior art and as relying upon "an effective amount of the combination ...", which is ill-defined and wherein applicant's assertions appear inconsistent with the instant disclosure as filed and the prior art teachings of the broadest reasonable interpretation of the claimed methods and limitations.

11. No claims are allowed.

Art Unit: 1644

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, Ph.D., J.D.  
Primary Examiner  
Technology Center 1600  
March 2, 2007